# Hemoglobinopathies

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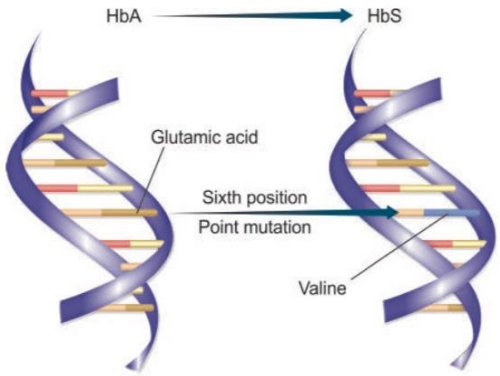
It's a family of genetic disorders caused by production of a structurally abnormal hemoglobin molecule, synthesis of insufficient quantities of normal hemoglobin or both.

- So, abnormalities occur in:
- Structure of the globin chain (ex: sickle cell disease).
- Globin chain production (ex: thalassaemia).

## Sickle Cell Anemia

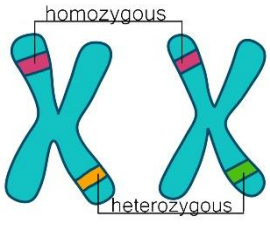
The sickle cell disease is a type of hemolytic anemia caused by a single base mutation (point mutation) in the β-globin gene that changes the sixth amino acid from glutamic acid to valine.




## Classification of sickle cell disease

### Sickle cell anemia (SS)

- Homozygous state—both β-globin chains are abnormal/defective.




### Sickle cell trait (AS)

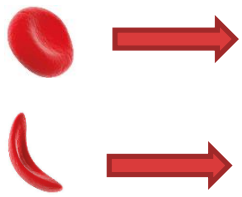
- Heterozygous state—one gene allele is defective (for HbS) and while the other gene allele is normal (for HbA).

## Pathogenesis

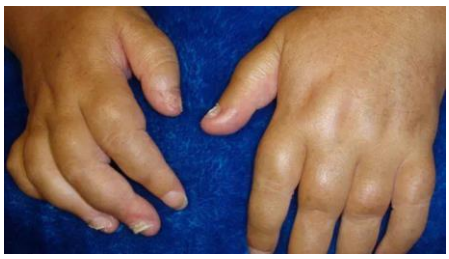
When HbS is deoxygenated, the molecules of haemoglobin polymerise to form pseudocrystalline structures known as 'tactoids'. These distort the red cell membrane and produce characteristic sickle-shaped cells.

## Clinical features

The disease usually does not manifest itself until the 6 months of age. irreversibly sickled cells have a shortened survival and plug vessels in the microcirculation .




### Vaso-occlusive crisis



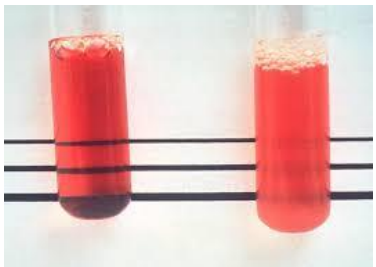
Plugging of small vessels in the bone produces acute severe bone pain. This affects areas of active marrow: the hands and feet in children ( called dactylitis ) or the femur, humerus, ribs, pelvis and vertebrae in adults.

Patients usually have systemic response with tachycardia , sweating and fever. This is the most common form of crisis .

## Investigations

- Hb (6-8 g/dl)
- Blood film (sickle cells and increase in reticulocyte count to 10-20%)
- Sickle solubility test.

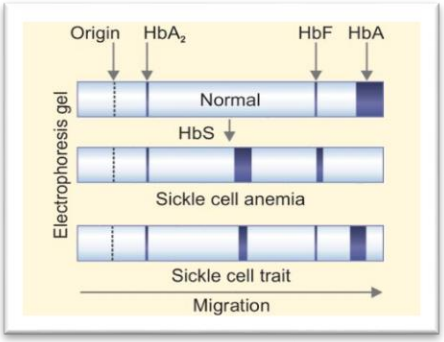
  A mixture of HbS in a reducing solution such as sodiumdithionite gives a turbid appearance because of precipitation of HbS, where as normal HbA gives a clear solution.



❖ Hb electrophoresis (the definitive diagnosis):

-No HbA band and predominance of HbS (homozygote).

-HbA and HbS bands (sickle cell trait) (heterozygote).

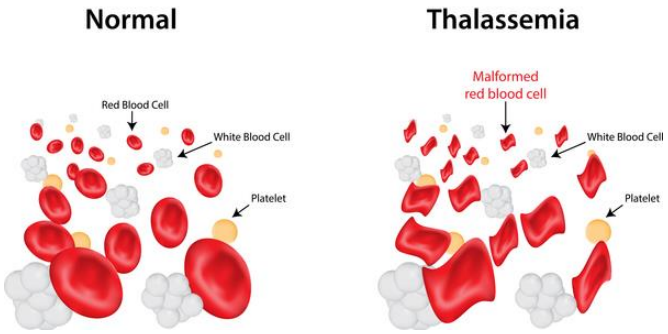



## Treatment

- All patients with sickle-cell disease should receive prophylaxis with daily folic acid.
- Vaso-occlusive crises are managed by aggressive rehydration, oxygen therapy, adequate analgesia and antibiotics.
- Regular Transfusion to suppress HbS , for patient with recurrent severe complications

## Thalassemias

They are hereditary haemolytic diseases in which there is a reduced rate of production of one or more of the globin chains of Hb. This basic defect results in imbalanced globin chain synthesis




## Classification

Thalassemia is classified according to which globin chain is produced in reduced amounts into:

### α-thalassemia

It results from deletion of one or more of the four gene alleles coding for the α globin chain in Hb.

**Clinical syndromes associated with α-thalassemia**

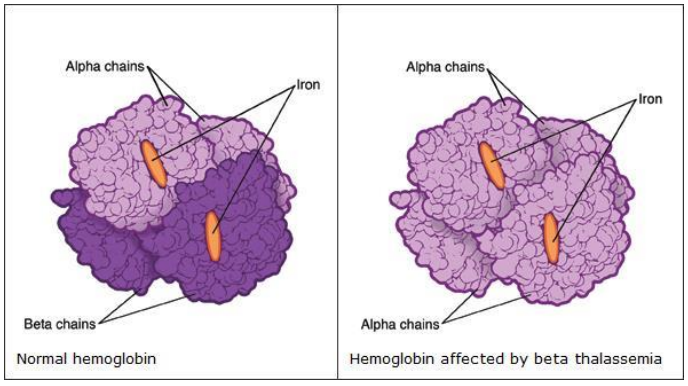
| Clinical syndrome | No . of α-globin genes deleted | Clinicopathological features |
|---|---|---|
| **Silent carrier state** | **1** | **A symptomatic** |
| **α-thalassemia trait** | **2** | **Usually a symptomatic, Normal Hb or minimal anemia.** |
| **Hemoglobin H disease** | **3** | **Moderate anemia** |
| **Hydrops fetalis** | **4** | **Severe form ,fatal and usually results in intrauterine death.** |

## β-thalassemia

Point mutation in the β globin gene resulting in reduced or absent synthesis of β globin chain , it's the most common type of thalassemia.

The β-thalassemias can be classified ,clinically, into three groups:

- Thalassemia minor : if one gene is affected , the person is a carrier and has mild anemia.
- Thalassemia intermedia : patients with thalassemia intermedia have varying effect of the disease ,mild anemia maybe their only symptom or they may need regular blood transfusions.
- Thalassemia major: is the most severe form of β thalassemia. It develops when β globin genes are missing.



## Clinical features of β-thalassemia major

- Patient presents within the first year of life with failure to grow, poor feeding ,recurrent attacks of infection .
- On examination: the patient is pale, jaundiced with hepatosplenomegaly.

## Investigations

- Hb 2-8 g/dl
- Blood film : microcytic hypochromic anemia with reticulocytosis.
- Hb Electrophoresis: The HbF level is always elevated, In thalassemia major : only HbF and HbA2 (no HbA1).
- HPLC ( High Performance Liquid Chromatography) is used to separate and quantify various normal and abnormal Hb.

## Treatment

α thalassemia

- No treatment needed for α thalassemia trait
- Transfusion for Hemoglobin H disease.

β thalassemia

- No treatment is needed for β thalassemia minor
- Transfusion/ bone marrow transplantation for β thalassemia major.